REMARKS

Status of the Claims

Claims 2-13, 17-19 and 22-44 and are currently pending in the application. Claims 2-13, 17-19 and 22-40 stand rejected. Claims 2, 3 and 40 have been amended as set forth herein without prejudice or disclaimer. New claims 41 and 42 have been added herein. No new matter has been added by way of the present amendments. Specifically, the amendments to claims 2 and 3, parts (d) are supported by the specification at, for instance, page 7, lines 19-22. New claims 41 and 42 are supported throughout the specification and by claim 40. New claim 43 is supported by the specification at, for instance, page 5, lines 14-27. New claim 44 is supported by the specification at, for instance, Example 1, pages 11-12. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 40 stands rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. (*See*, Office Action of February 9, 2007, at page 2, hereinafter, "Office Action"). Applicants traverse the rejection as set forth herein.

The Examiner states that the Declaration is not commensurate in scope with the claim and thus is ineffective with respect to those compositions not tested, that the specification does not enable the treatment of skin cancer and herpes, and that the translation of the Watzl reference submitted is insufficient. (*Id.* at pages 4-5). However, the Examiner states that the specification does enable the treatment of the remaining problems, including skin irritation, sun burn,

cellulites, wrinkes, acne, neurodermatitis, ozone damage, burns, caustic burns, thickening, edemas, hematomas and hemorrhoids. (*Id.* at page 2).

Although Applicant does not agree that claim 40 lacks enablement, to expedite prosecution, claim 40 has been amended herein without prejudice or disclaimer to remove the terms herpes and skin cancer.

Furthermore, since new claims 41 and 42 are now directed to the subject matter removed from claim 40, the following additional comments are provided to traverse the Examiner's comments concerning the basis for the rejection of claim 40 as lacking enablement.

The Examiner maintains that the specification does not reasonably provide enablement for the treatment of skin cancer and herpes. The Examiner is respectfully requested to carefully reconsider the presently claimed invention and the arguments filed in Applicant's last response of December 29, 2006. That is, on page 3 in the section "Guidance of the Specification" the Examiner points to "arthrosis" and "rheumatism" although these diseases were previously deleted in present claim 40. Thus, it appears the Examiner has simply "copied and pasted" the comments from the prior Office Action of November 30, 2005 without actually considering the presently pending claims, nor the amendments and arguments presented in Applicant's reply of December 29, 2006. The Examiner is urged to timely review the actual claims pending and Applicant's comments of December 29, 2006 in addition to the following comments.

The Examiner also indicates that the application does not contain a working example specifically directed to the treatment of divergent skin disorders such as skin cancer. The Examiner acknowledges that all working examples provided by the specification are directed towards the improvement of microcirculation, but the Examiner apparently continues to miss that

this is the core of the presently claimed invention. As repeatedly emphasized in prior replies, **the core of the invention is the improvement of the microcirculation of the cells**. The inventive preparations use the principle of ion exchange between cell interior and cell exterior using high osmotic pressure, which is created by the combination of active substances of the inventive preparation. In this process, for example, the amino acid(s) in combination with zinc oxide and inorganic peroxide help the ions to more effectively overcome the natural barriers of the cell membranes to reach the cell interior which is the actual site of action, which, therefore, plays an important role for the treatment of diseases.

By the improvement of microcirculation of the cell the other effective substances such as a secondary plant substance (SPS) can more effectively be infiltrated into the cells and, therefore, more effectively provide their pharmaceutical effects (cf. page 5 of the present specification). Example 1 may be regarded as a basic preparation of the present invention, which is also effective for treating skin cancer. As clearly indicated in the last paragraph of Example 1 of the present specification, this preparation significantly improves the microcirculation of cells. The improvement of microcirculation is a key feature for the treatment of the indicated disorders and diseases and, therefore, also for the treatment of skin cancer and herpes.

In the last two paragraphs of page 4 of the Office Action the Examiner indicates that the Applicant's arguments filed on December 29, 2005 have been considered. Applicant requests clarification of the record in that Applicant's last reply was actually submitted December 29, 2006. The last paragraph on page 4 indicates that the Examiner notes that Applicant has not provided the IDS citing Watzl et al., nor has Applicant provided page 250, the Table to which the Applicant refers. Enclosed herewith is an English language translation of this table. This

English language translation is obtained from the internet. This table clearly points to "Watzl & Leitzmann, 1995" which is the same reference from which the Table in question has been provided previously. Therefore, Applicant is of the opinion that it is not necessary to file a certified English translation of this table. Furthermore, Applicant emphasizes that an English translation of the German version of this table is not necessary since the technical terms used in the German language table are very similar in the English language and, therefore, easily can be understood by a person skilled in the art who is not familiar with the German language.

Furthermore, as already communicated to the Examiner in the reply dated December 29, 2006, page 10, 2nd paragraph, Watzl et al. is a book having 250 pages and, therefore, that a full verified English language translation of this book would be an undue burden for the Applicant.

On page 5, 1st paragraph "the Examiner points out the instant claims are not directed to any specific weight percent of the plant substance." However, it is noted that many patents on the technical field of the present application have been granted wherein the claims do not contain any specific weight ranges of the claimed substances. In these other issued patents in this field,it is sufficient that the specification provides an indication of useful weight ranges. The present application contains such an indication on page 8, 3rd paragraph.

At page 5, 1st paragraph, of the Office Action, it is indicated that "the Examiner cannot determine if [Watzl] teaches a concentration of the plant substances that needs to be utilized to provide the anticarcinogenic effect." However, it is entirely irrelevant for the present invention whether the Watzl et al. reference describes any concentrations of plant substances needed to be utilized to provide an anticarcinogenic effect since, as already emphasized in Applicant's previous replies, the Watzl et al. reference is based on the field of nutrition. That is, the nutrients

described in Watzl et al. are only administered orally. If the Watzl et al. reference should contain any hint with respect to concentrations of SPS used for oral administration, such an indication cannot be simply transferred to preparations to be topically administered, as is known to a person of general skill in the art. Therefore, again, it is irrelevant whether Watzl et al. provides any weight ranges for SPS.

The Inventor further emphasizes that it is not necessary to file any further pages of the Watzl et al. reference since the table itself is self-explanatory and provides all the information necessary for enablement. The Watzl et al. table has been filed for the purpose of clearly demonstrating that the effects of SPS *per se* are known to a person skilled in the art. As can be seen from the enclosed table, it was known in 1995 in the technical field of nutrition that, e.g., carotenoids, phytosterins, polyphenols and the like have anticarcinogenic effects, that, e.g., saponins, glucosinolates and polyphenols have antimicrobial effects and so on.

Therefore, the Watzl et al. table clearly enables a person skilled in the art to specifically select those SPSs useful for the treatment of a specific disease such as skin cancer and herpes. That is, the Watzl et al. table has been submitted solely for the purpose of refuting the Examiner's allegation that a person skilled in the art cannot select appropriate SPSs.

Additionally, it is important to note that the Inventor is the first person to use SPSs in combination with the other components of the claimed preparation in a preparation for topical administration.

The Examiner states that the instant invention requires undue experimentation for a skilled person to practice the invention. Applicant respectfully disagrees. The specification provides sufficient information for selecting the appropriate components of a recipe for also

treating skin cancel and herpes. As mentioned above, page 8, 3rd paragraph of the specification points to specific groups of useful SPSs and a preferred weight range thereof. The table of the Watzl et al. reference previously submitted contains the same groups of SPSs and provides information with respect to (proof of) desired effects. Furthermore, it is quite routine in the technical field of pharmacy that a basic recipe has to be further adapted with respect to the used weight ranges of each component in order to provide optimum effects. This, however, is routine and not "undue" experimentation as alleged by the Examiner. Therefore, a person skilled in the technical field of the present invention can carry out the invention also with respect to the treatment of skin cancer and herpes using the information provided by the application and the general knowledge of the field. Experiments for providing optimum effects of a basic recipe are typical and routine in this technical field and also part of European-wide marketing approval of pharmaceutical compositions.

Therefore, reconsideration and withdrawal of the enablement rejection of claim 40 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Schinitsky & Oliver

Claims 2, 5-11, 17-19 and 26-40 stand rejected in light of the combined disclosure of newly cited reference Schinitsky, EP 0281812 (hereinafter, "Schinitsky") and Oliver, U.S. Patent No. 5,869,062 (hereinafter, "Oliver"). (*Id.* at page 9). Applicants traverse the rejection as hereinafter set forth.

The Examiner states that the disclosure of Schinitsky is relied upon to show a preparation for treating acne comprising a keratolytic agent, an astringent (such as zinc oxide), and an anti-inflammatory agent (such as amino acids). (*Id.* at page 10). The Examiner states that Schinitsky suggests that amino acids are "known to have anti-inflammatory activity." (*Id.*). The Examiner cites to, for example, column 6 of Schinitsky which discloses or suggests the use of cysteine in a preparation for treating acne. (*Id.*). The Examiner states that because the present claims recite "terpenes" (for instance, claims 2 and 3, part (d)), Oliver makes such claims obvious because Oliver discloses or suggests tea tree oil which includes terpenes. (*Id.*). The Examiner considers the hydrogen peroxide disclosed in Oliver to be an inorganic peroxide. (*Id.* at page 10). The Examiner states that Oliver discloses or suggests golden seal extract, which itself includes several minerals and salts. (*Id.*). Furthermore, the Examiner notes that calamine, also suggested by Oliver, comprises two types of salts: zinc oxide and ferric oxide. (*Id.*). The Examiner also points out that Oliver discloses the combination of hydrogen peroxide, and other peroxides, with 18% zinc oxide. (*Id.*, at page 6).

Although Applicants do not agree that the claims are obvious in light of the cited references, to expedite prosecution, part (d) of claims 2 and 3 has been amended without prejudice or disclaimer to recite, in part, "2 to 50% by weight, based on the sum of all components in the preparation" as an amount of SPS to be included. Therefore, the amended claims are directed to a preparation for topical application comprising:

> (a) at least one salt selected from alkali metal salts, alkaline earth metal salts and other minerals,
> (b) at least one individual amino acid in pure form,
> (c) zinc oxide and an inorganic peroxide, and
> (d) 2 to 50 wt.-% of at least one secondary plant substance selected from a specific group;

and (claim 3): (e) at least one polyunsaturated fatty acid of vegetable sources.

Distinguishing Features of the Presently Claimed Invention Over the Cited References

Schinitski, EP 0281812

Schinitski describes a composition for treatment of acne comprising a keratolytic agent, an astringent, and an anti-inflammatory agent. (*See*, for example, Schinitski, claim 1). The keratolytic agents can be selected from salicylic acid, retinoic acid, resorcinol, treponin, sulphur, benzoic acid, urea and benzoyl peroxide. (*See*, *Id.* at column 4, lines 19 to 22 and claim 2). Representative astringents include zinc oxide, aluminum chloride, aluminum acetate, calamine, zinc acetate, zinc sulphate and zinc chloride. (*See*, *Id.* at column 5, 3rd paragraph and claim 6). The anti-inflammatory agent includes non-steroidal compounds including anti-inflammatory amino acids, amino sugars, and non-steroidal prostaglandin synthesase inhibitors such as Ibuprofen. (*See*, *Id.* at column 5, lines 41 to 45). Schinitski suggests in column 5, line 54 to column 6, line 2 that, if benzoyl peroxide is selected for the preparation of a composition, a stronger anti-inflammatory agent such as hydrocortisone or non-steroidal anti-inflammatory agents such as ibuprofen can be used advantageously. Schinitski clearly discloses in column 3, lines 23 to 27 that there is no need to use active ingredients having anti-bacterial characteristics.

Therefore, it is an object of Schinitski to provide a novel therapeutic approach for the treatment of acne that does not rely on topical antibiotic-containing preparations. (*See*, *Id.* at column 3, lines 41 to 46). Schinitski also emphasizes in column 3, line 41 to column 4, line 13 that its composition for the treatment of acne comprises an anti-inflammatory agent, an astringent and a keratolytic agent, and that it is these three mechanisms which constitute the

rationale of the therapeutic treatment scheme and which dictate the three types of ingredients selected for the formulation and method of treatment.

Oliver (U.S. Patent No. 5,869,062)

Oliver describes a method for the treatment of skin acne comprising the steps of applying a composition directly to the skin comprising a base in an amount between about 25 and 60 wt. %, calamine in an amount between about 8 and 20 wt. %, an anti-oxidant in an amount between about 0.5 and 3 wt. %, and a herbal anti-bacterial product in an amount between about 0.25 and 4 wt. %. (*See*, Oliver, claim 1). The skin treatment composition of Oliver includes calamine which is zinc oxide with about 0.5 % ferric oxide. The purpose of the calamine is to reduce inflammation, redness and itching. (*See, Id.* at column 2, lines 14 to 19). Anti-oxidants are described in Oliver. (*See, Id.* at column 2, lines 20 to 27). The naturally occurring anti-bacterial product disclosed in Oliver is for treating any infections that may arise. Suitable anti-bacterial products according to Oliver include naturally occurring herbs selected from golden seal extract, tea-tree oil, echinacea, garlic, and red clover. The tea-free oil of Oliver is used in an amount of 1 to 3 wt. %. (*See, Id.* at column 2, lines 28 to 38). The key components of golden seal extract are choline, cholcogenic acid and B-complex, since they function to facilitate the infection-fighting ability of the herbal ingredients. (*See, Id.* at column 2, lines 39 to 46). Oliver discloses in column 3, 2nd paragraph that a peroxide may also be used in an amount between about 3 and 8 percent. Suitable peroxides include hydrogen peroxide. The purpose of including a peroxide component is to help treating any infection. The peroxide may also be selected from benzoyl

peroxide, acetyl peroxide, t-butyl peroxide, para-chlorobenzoyl peroxide, and methyl ethyl ketone peroxide. The table in column 3 of Oliver only discloses "Peroxide 3 % strength."

Amended claim 2 comprises as a component, (c) zinc oxide and an inorganic peroxide. On page 6, 2nd paragraph, last sentence of the Office Action, the Examiner alleges that "Oliver clearly suggests the use of hydrogen peroxide and prefers its use." The Examiner misinterprets the disclosure of Oliver in this sense. That is, Oliver describes, at column 3, 2nd paragraph, useful peroxides such as hydrogen peroxide and five specific organic peroxides, as mentioned above. However, this passage in Oliver does not disclose preference for any peroxide in particular. This conclusion is also supported by claim 15 of Oliver. The table in column 3 of Oliver only describes "Peroxide 3 % strength" without further describing which peroxide was actually used. (*See, Id.* at also column 1, lines 49 and 50, and column 3, lines 38 to 40). Therefore, the Examiner misstates the disclosure of Oliver in concluding that Oliver teaches a preferred use of hydrogen peroxide. In fact, Oliver teaches six different peroxides, wherein five peroxides thereof are clearly organic peroxides and the remaining is hydrogen peroxide. This suggests a preference for organic peroxides. Organic peroxides, however, are not encompassed by the presently pending claims of the present invention.

The preparation according to amended claims 2 and 3 of the presently claimed invention further comprise 2 to 50 wt. % of at least one secondary plant substance (d) selected from a specific list. In contrast, the composition of Oliver comprises naturally occurring anti-bacterial products selected from golden seal extract, tea-tree oil, echinacea, garlic and red clover. (*See, Id.* at column 2, lines 29 to 46). It should be emphasized that Oliver only describes herbs for providing the anti-bacterial product. Oliver neither discloses nor suggests which components of

the herbs are responsible for the desired effects. Oliver neither describes any specific amount or quantity in which the effective components of the used herbs should be present in the composition. For example, Oliver only teaches the use of 1 to 3 wt. % tea-tree oil, without further describing the ingredients and effective components and amounts thereof of the used tea-tree oil.

In fact, in contrast to the presently claimed invention, Oliver does not particularly teach or suggest the use of secondary plant substances and any effects thereof. Therefore, Oliver neither discloses nor suggests the use of secondary plant substances for topical preparations. Additionally, the Examiner states at page 9, lines 9 and 8 from the bottom of the Office Action: "1-3 % tea-tree oil (contains terpenes)." However, the term "(contains terpenes)" is not present in the disclosure of Oliver but has been added by the Examiner in light of the knowledge of the subject matter disclosed in the present invention. Whether the tea-tree oil contains terpenes or not is a matter of novelty, but not a matter of inventive step if Oliver does not explicitly contain this indication.

Finally, and importantly, Oliver is absolutely silent with respect to the use of secondary plant substances (SPSs). If the Examiner disagrees, the Examiner is requested to clearly identify those passages of Oliver that disclose or suggest the use of SPSs. Although it may be correct that tea-tree oil contains terpenes, Oliver does not disclose this information and particularly does not disclose or suggest which of the components contained in said oil the desired effects are based. According to Römpp Lexikon, "Chemie", Thieme Verlag, which is a standard textbook, tea-tree oil can contain up to 40 % terpinene-4-ol, depending on the specific kind of herb. That is, 60 % of the oil is not terpene but other components and chemicals. Again, Oliver does not

disclose any specific ingredients and amounts of these ingredients, as recited in the presently claimed invention. That is, there is nothing in Oliver that would make it obvious to a person skilled in the art which component of the tea-tree oil has the desired effect. Therefore, Oliver cannot make obvious presently claimed SPSs. It should also be noted that, considering the maximum amount of terpenes in tea-tree oil, Oliver neither discloses nor suggests the use of at least 2 wt. % of at least one secondary plant substance, either.

Besides tea-tree oil, Oliver also describes further examples useful as anti-bacterial products. In column 2, lines 39 to 46, Oliver describes golden seal extract and the ingredients thereof. The described list of ingredients does not contain any SPS. The other examples for the antibacterial product are not further described and, therefore, Oliver does not provide any insight at all as to the effective component used. Clearly, Oliver neither discloses nor suggests any SPS which, contrary to Oliver, are specifically used as essential component (d) in a preparation for topical application of the presently claimed invention.

Again, as previously commented upon in prior replies, Oliver does not disclose nor suggest how the object of the present invention, namely, the improvement of microcirculation, can be solved or achieved. Furthermore, Oliver is silent with respect to the use of any SPS, advantages and effects thereof, and amounts to be used thereof, as presently claimed in the present invention. Any allegation that Oliver even suggests the use of SPS can only be made based on hindsight reconstruction using the knowledge disclosed by the present invention. Furthermore, Oliver is silent concerning the use of any individual amino acid in pure form as required by the present invention.

Schinitski & Oliver Combined

The Examiner alleges, at page 10 of the Office Action, that the subject matter of the present invention is obvious from a combination of Oliver and Schinitski. However, as discussed above with respect to the Oliver disclosure, Oliver is silent with respect to the use of any SPS. That is, since Oliver does not provide any disclosure or suggestion pointing to the use of SPS (since it does not describe the effective components of the used herbs) Oliver cannot suggest the use of SPS and particularly in an amount of at least 2 wt. %, as presently claimed. Oliver is also silent with respect to the use of individual amino acids in pure form. Schinitski, on the other hand, although describing a composition of which the effects thereof are based on three possible mechanisms, namely, the use of an anti-inflammatory agent, an astringent and a keratolytic agent, clearly describes in the passages mentioned above that its therapeutic approach of treatment of acne condition is based on compositions not comprising anti-bacterial agents. This, however, is entirely inconsistent with the disclosure of Oliver, which clearly uses as one essential component, naturally occurring anti-bacterial products. Since the teachings of Oliver and Schinitski for this reason are contrary to each other, there is no motivation for a person skilled in the art to combine Oliver with Schinitski. Even upon doing so, one of skill in the art could not possibly predict the potential outcome of such a combination.

Furthermore, the disclosure of Schinitski clearly teaches away from the presently claimed invention. That is, at column 5, line 54 to column 6, line 2 of Schinitski clearly discloses that, if benzoyl peroxide is used for the preparation of a composition, hydrocortisone or non-steroidal anti-flammatory agents such as ibuprofen should be used. This is a clear teaching against any amino acid if used in combination with a peroxide. Oliver can use zinc oxide and different

peroxides, one of which is benzoyl peroxide. A person skilled in the art, if he would combine Oliver and Schinitski at all, which is disputed, would first of all use benzoyl peroxide as the peroxide of choice since Schinitski also teaches the use of benzoyl peroxide. According to the teaching of Schinitski a person of skill in the art would then use hydrocortisone or ibuprofen thereby arriving at a preparation which is clearly not within the claims (no inorganic peroxide, no amino acid present).

Thus, the Examiner has failed to provide reasoning for the combination of these two references to arrive at the presently claimed composition. That is, while any number of possible compositions may be derived from combining the two references (although Applicant believes one of skill in the art would not combine the references for the reasons provided above), somehow the Examiner believes only Applicant's claimed composition would be derived. This is clearly an example of hindsight reconstruction because the disclosures of the two cited references are inapposite each other and actually point AWAY from Applicant's claimed compositions, as explained above.

A combination of Oliver and Schinitski does not make obvious the specific combination of ZnO, inorganic peroxide and individual amino acid since Schinitski, as mentioned above, clearly teaches away from the use of amino acids if the composition contains a peroxide, and instead clearly suggests stronger anti-inflammatory agents such as hydrocortisone or non-steroidal anti-inflammatory agents such as ibuprofen. For at least this reason, in addition to the other reasons discussed above, the skilled person would not add to the composition of Oliver any amino acids and would instead be clearly motivated by the Schinitsky disclosure to add stronger anti-inflammatory agents such as the proposed hydrocortisone or ibuprofen.

If the Examiner is not persuaded, the Examiner is respectfully requested to clearly identify those passages of Schinitski directing a person skilled in the art to use amino acids in a composition of Oliver, if this composition contains H_2O_2. In any case, neither the disclosure of Oliver nor the disclosure of Schinitski suggest the use of SPS in a preparation for topical administration.

A patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." (*See, Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 U.S.P.Q.2d 1373 (Fed. Cir. 2003)). Applicants are aware that while a reference must enable someone to practice the invention to anticipate the presently claimed invention under 35 U.S.C. § 102, a reference disclosing an inoperative embodiment may qualify as prior art for the purpose of determining obviousness under 35 U.S.C. § 103. (*See, Reading & Bates Constr. Co. v. Baker Energy Resources Corp.*, 223 U.S.P.Q. 1168 (Fed. Cir. 1985)). However, the paucity of disclosure with respect to the production of claimed compositions must be taken into consideration by the Examiner in determining obviousness. A reference that lacks an enabling disclosure may qualify as a prior art reference under 35 U.S.C. § 103, but only for what is disclosed in it, "[i]n order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." (*See, Beckman Instruments Inc. v. LKB Produkter AB*, 13 U.S.P.Q.2d 1301, 1304 (Fed. Cir. 1989), citing *In re Payne*, 606 F.2d 303, 314, 203 U.S.P.Q. 245, 255 (CCPA 1979)). Therefore, the disclosures cited by the Examiner do not make obvious the presently claimed compositions because the asserted goals of a reference, with nothing more, cannot block

patentability for one who actually achieves that goal. (*See also, Impax v. Aventis*, 468 F.3d 1366, Fed. Cir. 2006).

"However, as we recognized in *Rasmusson*, proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation. 413 F.3d 1326. That is, a section 102 prior art reference does not have to be "effective" to be enabling and thus anticipating. Id. Under Rasmusson, the effectiveness of the prior art is not relevant. Id. Rather, the proper issue is whether the '940 patent is enabling in the sense that it describes the claimed invention sufficiently to enable a person of ordinary skill in the art to carry out the invention." (*See, Impax v. Aventis*, 468 F.3d 1366, Fed. Cir. 2006). It is therefore submitted that the presently claimed invention cannot be obvious in light of the cited references because the cited references do not enable one of skill in the art to derive the presently claimed composition for the reasons provided above.

For at least the foregoing reasons, reconsideration and withdrawal of the obviousness rejection of claims 2, 5-11, 17-19 and 26-40 are respectfully requested.

Oliver & Horrobin et al. et al.

Claims 2-11, 13, 17-19 and 22-40 stand rejected in light of the combined disclosure of newly cited reference Oliver and Horrobin et al. et al., U.S. Patent No. 5,145,686 (hereinafter, "Horrobin et al. et al."). (*See*, Office Action, at page 11). Applicants traverse the rejection as hereinafter set forth.

In addition to the statements made concerning the disclosure of Oliver, the Examiner states that Horrobin et al. et al. is cited only for the disclosure or suggestion of the use of

polyunsaturated fatty acids and amino acids. (*Id.* at page 6). The Examiner concludes that Horrobin et al. et al., in combination with the disclosure of Oliver, disclose or suggest the claimed preparations, including the individual amino acids. (*Id.*).

Applicant first refers to comments provided in the Reply of December 29, 2006, at pages 18-22 and respectfully requests the Examiner again consider these points in addition to the following comments:

Differences Between the Disclosures of Oliver and Horrobin et al.

Contrary to Oliver, Horrobin et al. describe a composition not containing zinc oxide and an inorganic peroxide. The compositions of Oliver are particularly used for the treatment of acne whereas the compositions of Horrobin et al. et al. are used for the treatment of lesions of the skin or mucosal membranes. Contrary to the Examiner's contention, these purposes are clearly not identical and perhaps are incompatible.

That is, Horrobin et al. et al. describe a pharmaceutical composition for topical administration which comprises at least one physiologically acceptable lithium salt together with at least one substance selected from substances capable of selectively increasing the *in vivo* level of E-series prostaglandins, substances capable of inhibiting cyclooxygenase enzyme, substances capable of inhibiting the formation of lipoxygenase products, and lysine. (*See*, Horrobin et al., at column 1, lines 55 to 63). In columns 2 and 3 of Horrobin et al., there is described a multiplicity of different substances which could be used for increasing the *in vivo* level of E-series prostaglandins. For example, the *in vivo* level of E-series prostaglandins may be increased by incorporating dihomo-gamma-linoleic acid and its bioprecursors. Other examples are zinc salts,

ascorbic acid, spironolactone, rutin or other bioflavonoids, glutathione, eicosapentaenoic acid, vitamin E and further substances as disclosed in column 2, line 47 to column 3, line 56 of Horrobin et al. Thus, Horrobin et al. merely provide a long laundry list of a multiplicity of different substances that *could* be used for increasing the *in vivo* level of E-series prostaglandins.

In this passage, Horrobin et al. do not disclose or suggest any preference for the use of rutin and bioflavonoids. That is, Horrobin et al. do not provide any disclosure or suggestion to particularly select rutin or other bioflavenoids because of its advantages or effects thereof. Since Horrobin et al. is silent with respect to a combination of zinc oxide and inorganic peroxide, it is not obvious to a person skilled in the art that compounds disclosed in Horrobin et al. may be effective in a composition comprising particularly an inorganic peroxide or not. This would require undue experimentation and inventive activity. In the working examples of Horrobin et al., combinations of substances used for increasing the *in vivo* level of E-series prostaglandins are used. Table III of Horrobin et al., last line, points to rutin in an amount of 0.5 to 1 wt. %. That is, Horrobini et al. disclose or suggest only the use of very small amounts of rutin. The working examples of Horrobin et al. do not disclose or suggest any preference for the compounds used for increasing E-series prostaglandin levels.

Therefore, it is not obvious to a person skilled in the art which of the described compounds could be used in a theoretical composition according to Oliver, and whether the compound of Horrobin et al. would provide any advantage or improvement in such a composition of Oliver. From the combination of these references, it is also not obvious whether any new composition should contain one of the 5 organic peroxides or H_2O_2 disclosed in Oliver.

Besides of the multiplicity of compounds useful for increasing E-series prostaglandins, Horrobin et al. indicate in column 3, 1st paragraph that rutin and other bioflavenoids allegedly are capable of blocking the bioconversion of E-series prostaglandins to other prostaglandins. Column 3, lines 12 to 14 of Horrobin et al., however, describe that prostaglandins of the E-series only form a minor fraction of prostaglandin products of the metabolism of arachidonic acid. Since the major proportion of the prostaglandin products from arachidonic acid do not provide an anti-inflammatory action, it may therefore be desirable to incorporate into the compositions of Horrobin et al. a substance which is capable of selectively promoting the formation of E-series prostaglandins in the bioconversion of arachidonic acid. An example of a substance that may be used for this purpose is glutathione. (*See, Id.* at column 3, lines 12 to 30). This passage of Horrobin et al. provides a motivation for a person skilled in the art to use glutathione in a composition of Oliver, thereby again teaching away from the use of bioflavonoids. That is, the motivation to particularly select only bioflavonoids from the multiplicity of components disclosed in Horrobin et al. and to add bioflavonoids to a composition of Oliver can only be derived from Applicant's own disclosure of the present invention. Again, Applicant insists the Examiner is improperly using hindsight reconstruction to derive a single embodiment out of numerous possible embodiments, where no motivation exists to do so, and in some cases where the references actually teach away from doing so. The Examiner provides no basis either in the knowledge of one of skill in the art nor from the references themselves directing one of skill in the art to the presently claimed composition.

The third column, penultimate paragraph, of Horrobin et al. indicates that lysine may conveniently be present in the composition. However, surprisingly, there is no working example

in Horrobin et al. using lysine. Furthermore, Horrobin et al. do not point to any other amino acid besides lysine. There is absolutely no indication in the disclosure of Horrobin et al. that an amino acid, when specifically combined with zinc oxide and inorganic peroxide, could be used for improving the microcirculation of the cells of the skin, which is the object of the present invention.

Since Horrobin et al. do not use lysine in any working examples, and since Horrobin et al. do not provide any indication that lysine could provide any improving effects if combined with zinc oxide and an inorganic peroxide, as described in the present application, for instance at page 5, there is no motivation to specifically select lysine in a composition of Oliver. There is no disclosure anywhere in Oliver, either, that an inorganic peroxide could provide advantages in combination with lysine. Oliver teaches 5 organic peroxides and only one inorganic peroxide without giving any one peroxide a preference. Such an allegation of obviousness based on the disclosures of these references could only therefore be made in light of knowledge gained from the presently claimed invention.

As can be seen from the above, there is no motivation for a person skilled in the art to particularly select those components described in Horrobin et al. that are missing in the composition of Oliver to derive the subject matter of the presently claimed invention. As shown above, there is an unmanageable multiplicity of possibilities of combining the compounds disclosed in Oliver with the multiplicity of compounds disclosed in Horrobin et al. so that the subject matter of the application cannot be obvious from a combination of these references.

Furthermore, the Office Action, at page 6, last paragraph, indicates that "the Examiner points out that the instant claims are rejected under obviousness. The test for obviousness is not

whether the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." That is, the question to be answered is whether there is any teaching in the prior art as a whole (one or more documents) that would (not simply could) have prompted a person skilled in the art to modify or adapt the closest prior art using other prior art thereby arriving at a theoretical embodiment falling within the claims and thus achieving what the invention achieves. That is, the further prior art documents should contain a suggestion which prompts a person skilled in the art to modify a composition of Oliver such that the present invention is achieved. However, as clearly indicated above and also in our previous comments, there is nothing, neither in Schinitski nor in Horrobin et al., which prompts a person skilled in the art to specifically select those components missing in compositions of Oliver and add them to a composition of Oliver in the expectation of some improvement or advantage, particularly in expectation to solve the object of the invention. The Examiner has thus far not provided any disclosure that would direct a person of skill in the art in the direction of the Applicants' claimed invention. Furthermore, the Examiner has failed to take into consideration the unpredictability within the art. Since the cited references fail to disclose or suggest the biological effects or functions the various components, specific components, may have, the disclosures as a whole lack sufficient information upon which to base the selection of a theoretical composition (not disclosed by any references) that would make the presently claimed compositions obvious.

Again, the allegations of the Examiner that a person skilled in the art would add those components missing in Oliver in view of any teachings of Schinitski and Horrobin et al. can only be made in light of the knowledge disclosed by the presently claimed invention. As previously

argued at pages 17, 21 and 25 of the prior Reply of December 26, 2006, the Examiner is reminded of legal precedent barring hindsight reconstruction.

The Examiner is further respectfully reminded of legal precedent concerning the requirement of enablement of any references cited in support of an alleged obviousness rejection, as recited above, at pages 23-24. These legal precedents apply equally here in the present rejection over the disclosures of Oliver and Horrobin et al.

Reconsideration and withdrawal of the obviousness rejection of claims 2-11, 13, 17-19 and 22-40 are respectfully requested.

Murad, Oliver, Horrobin et al. et al. & Burke et al.

Claim 12 stands rejected in light of the combined disclosure of newly cited reference Murad, U.S. Patent No. 5,962,517 (hereinafter, "Murad"), Oliver, Horrobin et al. et al. and Burke et al., U.S. Patent No. 5,693,318 (hereinafter, "Burke et al."). (*See*, Office Action, at page 13). Applicants traverse the rejection as hereinafter set forth.

The Examiner states that the disclosure of Burke et al. is relied upon solely to show that the claimed peroxides and those disclosed in Oliver are functionally equivalent, according to the stating, "all function to disinfect the skin." (*Id.*). Regarding the lack of motivation to combine the disclosure of Burke et al. with that of Oliver, the Examiner states that both disclosures pertain to the disinfection of the skin, and thus are within the same "field of applicant's endeavor." (*Id.*).

However, Applicant respectfully refers the Examiner to the comments provided, above, with respect to the various combinations of the references that would not be motivated by one of skill in the art. Applicant again reiterates that, for similar reasons, among the myriad number of

combinations suggested by the combination of these FOUR references, there is absolutely no disclosure directing one of skill in the art to the particular embodiment presently claimed. Furthermore, the Examiner has failed to identify any such motivation in any of the cited references. Additionally, in light of the unpredictability within the art, and in light of the total lack of disclosure within the cited references attributing specific biological properties and advantageous functions of the various components of the presently claimed composition, it is respectfully submitted that the Examiner has failed to establish obviousness with respect to the presently claimed compositions. Even if, *arguendo*, the Examiner had found references specifically disclosing the exact ingredients of Applicants' composition, the references also fail to disclose the weight-percentages of the compositions, as recited in the presently amended claims.

Again, the allegations of the Examiner that a person skilled in the art would add those components missing in Oliver in view of any teachings of Schinitski and Horrobin et al. can only be made in light of the knowledge disclosed by the presently claimed invention. As previously argued at pages 17, 21 and 25 of the prior Reply of December 26, 2006, the Examiner is reminded of legal precedent barring hindsight reconstruction.

The Examiner is further respectfully reminded of legal precedent concerning the requirement of enablement of any references cited in support of an alleged obviousness rejection, as recited above, at pages 23-24. These legal precedent apply equally here in the present rejection over the disclosures of Oliver and Horrobin et al.

Reconsideration and withdrawal of the obviousness rejection of claim 12 are respectfully requested.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: August 8, 2007

Respectfully submitted,

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